Attachment 12: DEEM Memo

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Acute and Chronic Dietary Exposure and Risk Analysis for Methyl Parathion.
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Action Requested

A probabilistic Tier 3 (Monte-Carlo) acute dietary exposure and a chronic dietary exposure assessment for methyl parathion was requested to estimate the dietary risks associated with the reregistration of methyl parathion. It was requested that this acute assessment be done incorporating results from the United States Department of Agriculture's (USDA) Pesticide Data Program (PDP) when available. Methyl parathion residue estimates used in this assessment include percent crop treated estimates reported by Biological and Economic Analysis Division (BEAD) and are based primarily on three data sources: 1) USDA Pesticide Data Program food sampling data; 2) Food and Drug Administration (FDA) Surveillance Monitoring data; and 3) field trial data, submitted by the registrant to support tolerances.

Executive Summary

HED has completed a revision of the dietary risk assessment for methyl parathion using updated methods for estimating acute dietary exposure. Based on the deliberations of the Hazard Identification Assessment Review Committee (HIARC), hazard endpoints have been selected for both acute (one day) and chronic (long term) exposure intervals.

An uncertainty factor (UF) of 100 was applied to the risk assessment to account for inter- and intraspecies variability. The FQPA Safety Factor (as required by the Food Quality Protection Act of August, 1996) has been retained (10x) for the organophosphorous pesticide, methyl parathion.

The acute and chronic risk assessments were conducted for all methyl parathion food uses combined. Risk estimates are provided for the average U.S. population and various subgroups, with the major emphasis placed on the exposure estimates for infants and children. This assessment concludes that for all supported registered commodities, the acute risk estimates are above the Agency's level of concern (100% aPAD[1]) at the 99.9th percentile for the average U.S. population (378% of the aPAD) and all population subgroups. This assessment also concludes that for all commodities, the chronic risk estimates are below the Agency's level of concern (100% cPAD[1]) at the 99.9th percentile for the U.S. population (17% of the cPAD) and all population subgroups.

[1]aPAD/cPAD = acute/chronic Population Adjusted Dose = $\frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

Toxicological Information

The toxicological database is complete pending submission of a developmental neurotoxicity (DNT) study. In summary, methyl parathion is acutely toxic (category 1) for oral, dermal, and inhalation routes of exposure, is slightly-moderately irritating to the eyes and skin, and is not a dermal sensitizer. The toxicity endpoints selected for the risk assessment are based primarily on neurotoxic effects, including neuropathology and cholinesterase (ChE) inhibition in the brain, red blood cell (RBC), and plasma, as well as behavioral effects and systemic toxicity. A single exposure to methyl parathion (7.5 mg/kg) in rodents results in peripheral nerve demyelination (tibial and sural nerves, dorsal and ventral root fibers). Chronic exposure at a dose level of 2.21 mg/kg/day in rodents results in retinal degeneration and sciatic nerve degeneration. There are no notable differences in sensitivity to methyl parathion between male and female animals. No evidence of carcinogenicity was seen in any study. Methyl parathion is classified as a "Group E" carcinogen, indicating no evidence of carcinogenicity in humans; i.e., the chemical is characterized as "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is supported by the lack of mutagenic activity; however, there is evidence suggesting that methyl parathion may function as an endocrine disrupter.

Table 1: Revised Methyl Parathion Toxicological Endpoints

REVISED METHYL PARATHION ENDPOINTS 03/04/99				
Exposure Duration	**Exposure Route**	**Endpoint**		**Comments**
		Dose	**Effect**	
Acute - aPAD	Dietary	aPAD = 0.00011 mg/kg/d	Neuropathology and inhibition of brain, plasma, and RBC ChE	NOAEL = 0.11 mg/kg/d. Based on neurotoxicity, neuropathology and inhibition of brain, plasma, and RBC ChE occurring at 0.53 mg/kg/d. One year dietary study in rats. UF of 100 applied for intra and inter species differences and an additional safety factor of 10X retained by the FQPA Safety Factor Committee for FQPA.
Chronic - cPAD	Dietary	cPAD = 0.00002 mg/kg/d	Systemic toxicity, neuropathology, and inhibition of RBC ChE at the LOAEL	NOAEL = 0.02 mg/kg/d. Based on systemic toxicity, neuropathology, and RBC ChE inhibition occurring at 0.21 mg/kg/d. Inhibition of plasma and brain ChE occurred at higher doses. Retinal degeneration and clinical signs occurred at the highest dose. 2-Yr chronic feeding study in rats. UF of 100 applied for intra and inter species differences and an additional safety factor of 10X retained by the FQPA Safety Factor Committee for FQPA.

Residue Information

Methyl Parathion Usage:

Methyl parathion is registered for use (direct application during the growing season to the raw agricultural commodity) on a variety of fruits, vegetables, and feed crops. The published tolerances for methyl parathion are listed in 40 CFR §180.189.

Residue Estimates:

Dietary risk estimates are based, in part, on estimates of the percent usage of methyl parathion on each registered food commodity. BEAD estimated methyl parathion use (I. Yusuf and T. Kiely memo, 4/13/99) based on available pesticide survey usage data for the years 1987 through 1997. BEAD estimates are provided to HED as a weighted average, and as a maximum. To avoid underestimating exposure, this risk assessment assumed 1% crop treated for any BEAD estimate less than 1% (including zero), and also used the estimated maximum percent crop treated (%CT) for each commodity for both the acute and chronic risk assessments. Percent crop treated estimates varied from less than 1%CT to the highest level of 39%CT for peaches (Attachment 1 and 2).

Methyl parathion residue estimates, or anticipate residues (ARs) in this assessment are based primarily on three data sources: 1) field trial data, submitted by the registrant to support tolerances; 2) USDA Pesticide Data Program (PDP) food sampling data; and 3) Food and Drug Administration (FDA) Surveillance Monitoring data. The order of preference for the purpose of risk assessment is PDP data > FDA data > field trial data. PDP data are preferred over FDA data because the statistical design of the PDP program is specific for dietary risk assessment (i.e. sampling is done at grocery store distribution points instead of directly from the field), and because the foods are prepared before analysis as they would typically be before consumption (i.e. peeling, washing). Many methyl parathion treated commodities not sampled by the PDP program are assessed based on translation of data from PDP sampled commodities in the same crop group, FDA surveillance data, or field trial data. Field trial residue data are generally considered by HED as conservative or worse case scenario of possible residue and are more suited to the requirements of tolerance setting, because it requires highest rates of application and shortest PHI, than to the requirements of dietary risk assessment (when the most realistic estimate is desired).

When using crop field trial data in this assessment, all data were handled similarly except the data for cottonseed meal. Due to a low PHI for some special local needs (SLN) on cottonseed grown in Texas, the crop field trial studies were used for cottonseed meal incorporating Texas %CT for cotton grown in TX, and U.S. %CT for cotton grown in all other states so as to not overestimate the risk (Attachment 2).

Acute Assessment:

Single Serving Commodities with PDP/FDA Detections: The PDP and FDA databases report most detected residues as residues found in 5 lb. composite samples. This manner of reporting may not be representative of possible high-end residues that could be found if individual units of fruits and vegetables were analyzed. This assessment uses a statistical methodology for applying existing (composite) information to acute dietary risk assessments. This methodology consists of extrapolating data on pesticide residues in composite samples of fruits and vegetables to residue levels in single servings of fruits and vegetables. Given the composite sample mean**,** the composite sample variance, the number of units in each composite sample, and assuming a lognormal distribution, it is possible to *estimate* the mean and variance of the pesticide residues present on single servings of fruits and vegetables. These parameters can then be applied to generate information on the level of residue in fruits and vegetables (and calculate a theoretical distribution). This information was incorporated into a probabilistic exposure estimation model, the Monte-Carlo method. This methodology has a higher degree of accuracy when more than 30 composite samples have detectable residues (Use of Pesticide Data Program in Acute Risk Assessment - sent to Federal Register May,1999). Commodities that are blended (such as grains) or are smaller than single unit servings (peas) were not decomposited since the measured PDP levels were assumed representative of the actual range of residue.

Chronic Assessment:

For chronic risk assessment, reported residues were averaged, whether based on PDP, FDA, or field trials. If a commodity had no reported detections by the PDP and FDA programs, and the expectation of no detection was confirmed by field trial data, the weighted average of the Limits of Detection (LOD) were used to account for possible exposure that could not be more precisely quantified (½ LOD methyl parathion + ½ LOD methyl paraoxon).

Methyl Paraoxon:

This assessment assumes that methyl paraoxon is equal in toxicity to the parent methyl parathion and accounts for the possibility of this metabolite occurring in treated foods. In general, field trial studies have included analysis for methyl paraoxon, as have FDA surveillance data. The PDP program did not analyze for methyl paraoxon (1994-1998). For the commodities in which methyl paraoxon was detected in the field trial analyses, but not detected by FDA surveillance, paraoxon is accounted for by an assumption of ½ LOD. For commodities with no detection of methyl paraoxon in FDA or field trial data, the assumption was zero residue, and ½ LOD was not incorporated.

Processing Factors:

Methyl parathion residues may be either concentrated or reduced by the activities of drying (prunes etc.), processing (juice, catsup etc.), washing, peeling, and cooking. If methyl parathion was measured prior to any of these processes, the predicted effect of the process has been applied to the estimated final residue at consumption. This assessment used factors to account for various processing, but most significantly, for the effect of cooking. This assessment reduced all food-forms designated as boiled or canned by a factor of 95% (0.05), which was established in a submitted canned snap bean study (MRID 44812901). Other processing factors (Methyl Parathion Residue Chemistry Chapter; REV. 5/99; Bonnie Cropp-Kohlligian; May 12, 1999; D255926) including DEEM™ default factors that were used in this assessment are listed in attachment 2.

Consumption Data and Dietary Risk Analysis

The DEEM™ Program: HED is currently using software developed by Novigen Sciences, Inc., named the *Dietary Exposure Evaluation Model* , or DEEM™ , to calculate acute and chronic dietary risk estimates for the general U.S. population and various population subgroups. The food consumption data used in the program are taken from the *USDA Continuing Survey of Food Intake by Individuals* (CSFII). The Agency is currently using 1989-92 consumption data. Consumption data are averaged for the entire U.S. population, and within population subgroups such as “all infants” to support chronic risk assessment, but retained as individual daily consumption data points to support acute risk assessment (which is based on distributions of consumption estimates for either deterministic- or probabilistic-type exposure estimates). The DEEM™ software is capable of calculating probabilistic (Monte Carlo) type risk assessments when appropriate residue data (distribution of residues) are available.

For acute risk assessments, one-day consumption data are summed and a food consumption distribution is calculated for each population subgroup of interest. The consumption distribution can be multiplied by a residue point estimate for a deterministic (Tier I/II type) exposure/risk assessment, or used with a residue distribution in a probabilistic (Monte Carlo) type risk assessment.

For chronic risk assessments, residue estimates for foods (e.g. apples) or food-forms (e.g. apple juice) of interest are multiplied by the averaged consumption estimate of each food/food-form of each population subgroup. Exposure estimates are expressed in mg/kg bw/d and as a percent of the cPAD.

Results and Discussion

Acute Probabilistic Exposure Analysis: (Monte-Carlo)

Based on the acute dietary exposure analysis as described above and using an aPAD of 0.00011 mg/kg/d, acute dietary exposure to all population subgroups exceeds the aPAD at the 99.9th exposure percentile (see Table 2). Estimated methyl parathion exposure to infants and children, as well as the general U.S. population, also exceeds the aPAD at the 99th percentile. Children 1-6 years have been identified as the most highly exposed population subgroup. Estimated acute dietary exposure to children 1-6 years exceeds the aPAD at the 95th, 99th, and 99.9th exposure percentiles. A complete listing of the acute dietary results are in attachment 4.

Several crops have been identified as making significant contributions to the dietary risk. Residues measured on these crops and the surveyed consumption of these crops, factored together, results in these crops taking up a significant percentage of the aPAD and thereby, making significant contributions to the risk. Theoretically, the overall risk exceeds the Agency's level of concern when the aggregate risk (food + water + residential) $\geq$ 100% PAD. A number of crops had significant residues from PDP data and are high consumption items (e.g. peaches, apples). The significant acute contributors have been identified as apples, cottonseed, peaches, grapes, and pears. Apples and peaches alone exceed the Agency's level of concern. For all the significant contributors, except cottonseed oil, PDP and/or FDA monitoring data have shown measurable residues of methyl parathion, some greater than half the tolerance. The FDA monitoring data used for cottonseed oil showed no detectable residues; however, there were only two samples of oil analyzed. The Agency believed that residues are not likely to be found in cottonseed oil since there are no detectable residues found in seed. Therefore, FDA monitoring data were used so as not to overestimate the potential risk from cottonseed oil.

The acute summary table below shows the acute dietary risks to the U.S. population, infants, and children from exposures to all the supported crops. A complete listing of the acute dietary results are in attachment 4.

Table 2: Acute Dietary Risk Estimates

Population	(95th percentile)		(99th percentile)		(99.9th percentile)	
	Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
U.S. Population	0.000044 mg/kg/day	40	0.000121 mg/kg/day	110	0.000416 mg/kg/day	378
All Infants <1 year	0.000095 mg/kg/day	86	0.000169 mg/kg/day	153	0.000415 mg/kg/day	377
Children 1-6 years	0.000132 mg/kg/day	**120**	0.000273 mg/kg/day	**249**	0.000969 mg/kg/day	**881**
Children 7-12 years	0.000061 mg/kg/day	55	0.000129 mg/kg/day	117	0.000428 mg/kg/day	388

Chronic Exposure Analysis:

Based on the chronic dietary exposure analysis as described above and using a cPAD of 0.00002 mg/kg/d, chronic dietary exposure to all population subgroups does not exceed the cPAD (see Table 3). Children 1-6 years have been identified as the most highly exposed population subgroup. The chronic summary table below shows the chronic dietary risks to the U.S. population, infants, and children from exposures to all the supported crops for which methyl parathion is registered. A complete listing of the chronic dietary results is in attachment 6. The chronic significant contributors have been identified as apples, peaches, grapes, cottonseed oil, and pears. For all the significant contributors, except cottonseed oil, PDP and/or FDA monitoring data have shown measurable residues of methyl parathion. The FDA monitoring data used for cottonseed oil showed no detectable residues; however, there were only two samples of oil analyzed. The Agency believed that residues are not likely to be found in cottonseed oil since there are no detectable residues found in seed. Therefore, FDA monitoring data were used so as not to overestimate the potential risk from cottonseed oil.

Table 3: Chronic Dietary Risk Estimates

Population	Exposure (mg/kg/day)	% Chronic PAD
U.S. Population	0.000003	17
All Infants (<1 year)	0.000006	29
Children 1-6 years	**0.000009**	**47**
Children 7-12 years	0.000005	22